UNITED STATES DEPARTMENT OF COMMERCE
Patent and Trademark Office

Address : COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231

SERIAL NUMBER | FILING DATE | FIRST NAMED APPLICANT | ATTORNEY DOCKET

SPENCER, I

EXAMINER

SPENCELEY BURN JOSAS AND LUBITZ
1880 CENTURY PARK EAST, FIFTH FLOOR
LOS ANGELES, CA 90067

151
ART UNIT | PAPER NUMBER
5

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 3/16/92 ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☒ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice re Patent Drawing, PTO-948.
3. ☐ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, Form PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____

Part II SUMMARY OF ACTION

1. ☒ Claims 1-19 are pending in the application.
   Of the above, claims 5-13 and 17-19 are withdrawn from consideration.
2. ☐ Claims _____ have been cancelled.
3. ☐ Claims _____ are allowed.
4. ☒ Claims 1-4 and 14-16 are rejected.
5. ☐ Claims _____ are objected to.
6. ☐ Claims _____ are subject to restriction or election requirement.
7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.
8. ☐ Formal drawings are required in response to this Office action.
9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable. ☐ not acceptable (see explanation or Notice re Patent Drawing, PTO-948).
10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____ has (have) been ☐ approved by the examiner. ☐ disapproved by the examiner (see explanation).
11. ☐ The proposed drawing correction, filed on _____, has been ☐ approved. ☐ disapproved (see explanation).
12. ☐ Acknowledgment is made of the claim for priority under U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____; filed on _____
13. ☐ Since this application appears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.
14. ☐ Other

EXAMINER'S ACTION

PTOL-326 (Rev. 9-89)

Applicant's election of Group I, claims 1-4 and 14-16 in Paper No. 4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (M.P.E.P. § 818.03(a)).

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

No enablement is seen for the production of antibodies, either monoclonal or polyclonal, that react with the protein of the invention or fragments thereof but do not cross-react with platelet derived growth factor (PDGF).

Claims 14-16 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

Claims 1-4 and 14-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The protein of the invention is inadequately identified in the claims. The mere recitation of a name, i.e. CTGF to describe the claimed invention is not sufficient to satisfy the statutes' requirement of adequately describing and setting forth the inventive concept. In order to avoid possible confusion over

proteins with the same or similar names that may be found to have patentably different structure and/or utility, proteins claimed by a particular name should be further distinguished in the claims by conventional protein characterization according to known parameters, such as by molecular weight, pI, amino acid sequence information, whether the protein is a monomer or multimer, function(s) and/or activity, and/or other finger-printing techniques such as IR, NMR, or UV spectroscopy data and/or other known properties which would serve to distinguish the claimed protein from other proteins. In addition, in consideration of the discrepancies often encountered in the art between protein molecular weights when determined by different methods, whenever a molecular weight is recited to characterize a protein the claim should include the method by which it was determined, i.e. whether by SDS-PAGE, gel filtration or some other method, and whether reducing or non-reducing (native) conditions were used. It must be identified so as to distinguish it from other proteins that might be similarly named. Further, the term "functional fragments" renders claim 1 indefinite for failing to a) define what is meant by functional, and b) failing to specify what fragments are encompassed by the claim. Claim 14 is indefinite for failing to define "specifically reactive", and is further indefinite for citing "fragments thereof".

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not

identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-4 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Matsuoka et al., or alternatively Campochiaro et al., or alternatively Shimokado et al.

Matsuoka et al. disclose the identification and purification of a PDGF-related protein of 34-36 kilodaltons (kD) from human wound fluid. The last paragraph of the first column, p. 4416 indicates that the peptides are biologically active as chemoattractants (e.g. chemotactic) and mitogens for connective tissue cells, and that they crossreact with anti-human PDGF IgG (antibodies). The paper does not specifically disclose that the protein is monomeric in nature, nor that it binds to PDGF receptors. However, as the disclosed 34-36 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Matsuoka et al.

Campochiaro et al. disclose the isolation of a PDGF-like protein from retinal pigment epithelial cells. Said protein has a relative mobility of 36-38 kD, is mitogenic and chemotactic, and binds to PDGF antibodies. The paper does not specifically disclose that the protein is monomeric in nature, nor that it binds to PDGF receptors. However, as the disclosed 36-38 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Campochiaro et al.

Shimokado et al. disclose the isolation of a PDGF-like protein of 37 kD, isolated from activated human alveolar and peritoneal macrophages. Said protein is mitogenic for connective tissue cells (p. 278), inhibited by anti-PDGF IgG (p.279) and competes for binding to PDGF receptors (paragraph bridging pages 279-280). The paper does not specifically disclose that the protein is monomeric in nature, nor that it has chemotactic properties. However, as the disclosed 37 kD protein appears to be identical to the CTGF of the current application, these characteristics are considered to be inherent to the protein disclosed by Shimokado et al.

Claims 1-4 are rejected under 35 U.S.C. § 102(a) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Ryseck et al.

Ryseck et al. disclose cloning and expression of fisp-12 from NIH 3T3 cells, a protein predicted to have 348 amino acids, with a predicted molecular weight of 37,792 daltons (p. 226, col. 2). A comparison of the amino acid sequences of fisp-12 and CTGF reveals only 13 discrepancies in the region between residues 86 and 392 (based on the numbering of Seq. ID No: 1)- see enclosed sequence comparison. There is greater divergence in the region preceeding residue 86. However, Ryseck et al. identify this region as a signal sequence, which would have no effect on the activity of the protein. At the time of their disclosure, Ryseck

et al. were unaware of the function of fisp-12, and made no mention of any ability to bind PDGF receptors. However, the degree of identity between the two proteins is such that the characteristics by which CTGF is claimed in Claims 1-4 are deemed by the Examiner to be inherent to fisp-12 in the absence of any evidence to the contrary.

Claims 14-16 are rejected under 35 U.S.C. § 103 as being unpatentable over Matsuoka et al., or alternatively Campochiaro et al., or alternatively Shimokado et al., or alternatively Ryseck et al. as cited in the rejections under 35 U.S.C. 102/103, above.

Having identified and purified the growth factor as demonstrated above, it would have been obvious to a person of ordinary skill in the art to generate antibodies specific to the growth factor and non-crossreactive with similar species for numerous reasons, including but not limited to a) to allow further study of the distribution and production of said growth factor, b) to aid in cloning said growth factor, c) to facilitate isolation of said growth factor from natural sources absent other related growth factors or e) for treatment of conditions relating to overproduction of the growth factor.
All of the above applications would have been immediately obvious to a person of ordinary skill in the art, as would the techniques necessary to generate the specific antibodies of the invention.

Any inquiry concerning this communication should be directed to Lorraine Spector, Ph.D. at telephone number (703) 308-4761.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist at telephone number (703) 308-0196.

LMS
752427.one
4/28/92

DAVID L. LACEY
SUPERVISORY PATENT EXAMINER
GROUP 180
4/28/92

FILE COPY

Serial Number 07/752427
Art Unit 1812

ATTACHMENT TO PAPER NUMBER: 5

COMPARISON OF THE CODING REGIONS OF FISP-12 AS DISCLOSED BY RYSECK ET AL. (CELL GROWTH DIFFER 2:225) AND CTGF, DISCLOSED BY APPLICANTS

```
nitial Score      =    306  Optimized Score   =    315  Significance =  0.00
esidue Identity   =    93%  Matches           =    305  Mismatches   =    22
aps               =      0  Conservative Substitutions                =     0
ranslation Frame=        1

   60      X  70        80        90        100       110       120
FVVLLALCSRPAVGQNCSGPCRCPDEPAPRCPAGVSLVLDGCGCCRVCAKQLGELCTERDPCDPHKGLFCDF
          || || ||  | |  | || |||||||||||||||||||||||||||||||||||||||||||
          PATGQDCSAQCQCAAEAAPHCPAGVSLVLDGCGCCRVCAKQLGELCTERDPCDPHKGLFCDF
          X       10        20        30        40        50        60
                         --> Signal

130       140       150       160       170       180       190
GSPANRKIGVCTAKDGAPCIFGGTVYRSGESFQSSCKYQCTCLDGAVGCMPLCSMDVRLPSPDCPFPRRVKL
||||||||||||||||||| ||| ||||||||||||||||||||||||| ||||||||||||||||||||||
GSPANRKIGVCTAKDGAPCVFGGSVYRSGESFQSSCKYQCTCLDGAVGCVPLCSMDVRLPSPDCPFPRRVKL
      70        80        90        100       110       120       130

200       210       220       230       240       250       260       270
PGKCCEEWVCDEPKDQTVVGPALAAYRLEDTFGPDPTMIRANCLVQTTEWSACSKTCGMGISTRVTNDNASC
||||| ||||||||| | |||||||||||||||||||| ||||||||||||||||||||||||||||||  |
PGKCCKEWVCDEPKDRTAVGPALAAYRLEDTFGPDPTMMRANCLVQTTEWSACSKTCGMGISTRVTNDNTFC
    140       150       160       170       180       190       200

     280       290       300       310       320       330       340
RLEKQSRLCMVRPCEADLEENIKKGKKCIRTPKISKPIKFELSGCTSMKTYRAKFCGVCTDGRCCTPHRTTT
|||||||||||||||||||||||||||||||||| || ||||||||| ||||||||||||||||||||||||
RLEKQSRLCMVRPCEADLEENIKKGKKCIRTPKIAKPVKFELSGCTSVKTYRAKFCGVCTDGRCCTPHRTTT
 210       220       230       240       250       260       270

    350       360       370       380       390 X     400
LPVEFKCPDGEVMKKNMMFIKTCACHYNCPGDNDIFESLYYRKMYGDMAXSQRVRDINS
||||||||||| |||||||||||||||||||||||||||||||||||||
LPVEFKCPDGEIMKKNMMFIKTCACHYNCPGDNDIFESLYYRKMYGDMA
280       290       300       310       320       X
```